Inappropriate Use of Antimicrobials and the Determinants among Patients Hospitalized in 3 Hospitals (Mizan, Bonga and Tepi) in Southwest Ethiopia

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Abstract

Background: The spread of antimicrobial resistance in developing countries is associated with complex and interconnected factors. Accordingly, there is poor controlling system in use of all the available antimicrobials in the hospital. This facilitates for the spread of inappropriateness of prescribing ending up with emergence and spread of antimicrobial resistance.

Objective: The study aims to assess the inappropriateness of the use of antimicrobials and the associated factors among patients admitted in 3 hospitals in southwest Ethiopia.

Methods: A prospective observational study design was employed at medical wards of 3 hospitals in southwest Ethiopia. Data was analyzed using SPSS, version 16.0 using logistic regression model. Statistical significance was considered at p-value <0.05.

Results: A total of 348 antimicrobial containing orders were prescribed for the 291 patients during the 2525 person-days of follow up. At least one antimicrobial use problem was identified among most (80.1%) of the patients. The multivariate logistic regression showed that the use of social drug [AOR=2.549(1.279-5.080) at 95% C.I.; p value=0.008], the use of antimicrobial in the previous 3 months [AOR=4.095(1.855-9.040) at 95% C.I.; p value=0.000] and the total number of drugs used [AOR=2.997(1.413-6.356); p value=0.004 for 3-4 drugs and AOR=4.653(1.985-10.906); p value=0.000 for ≥5 drugs at 95% C.I.] were independently associated with antimicrobial use problems.

Conclusion: At least one antimicrobial use problem was prevalent among most of the patients. The independent determinants of antimicrobial use problems were the total number of drugs used, use of social drugs and the previous use of antimicrobial.

Keywords: Inappropriate use; Antimicrobials; Southwest; Ethiopia

Introduction

Although many of infectious diseases can be prevented with improved personal hygiene, immunization and environmental sanitation, antimicrobials are still the main therapy for many of them [1]. World Health Organization (WHO) estimated that 80% of antibiotics is used in the community, of which about 20-50% is used inappropriately. As a result, WHO recommended involvement of the community in tackling of antibiotic resistance through improving access to medical services, reducing unnecessary use of antibiotics, taking a full course of treatment, not sharing medications with other people, and not keeping part of the course for another occasion [2,3].

Without effective antimicrobial, diverse fields of medicine will be severely hampered, including surgery, the care of premature infants, cancer chemotherapy, care of the critically ill and transplantation medicine [4]. Inappropriate use of antimicrobials leads to produce drug resistance which is one of the major issues. Inappropriate use of antibiotics can result in bacteria resistant to antibiotics in the community. The acceleration of antibiotic resistance and the decline in the development of new antibiotics to combat the problem has created a significant public health challenges to health policy makers, health care workers, and the population around the world [5,6].

Factors that promote the emergence of resistance include: frequent use of broad-spectrum antimicrobial agents, prolonged use of antimicrobial agents, more frequent use of invasive devices and procedures, large numbers of patients with complex medical problems in small areas within a hospital, and the presence of patients who require prolonged hospitalization [7]. Hospitals are considered an excellent compartment for the selection of resistant and Multi-Drug Resistant (MDR) bacteria [8]. The number of unqualified medical practitioners in any society is a big contributor of antimicrobial misuse [9]. For one thing, non-adherence to the guidelines frequently results in more broad-spectrum empirical therapy [10]. Moreover, approximately 5% of hospitalized patients who were given antimicrobials experienced some adverse reactions to these drugs for which 20% required treatment [11].

The early switch from intravenous to oral treatment is feasible and also advantageous in: narrowing spectrum of action, preventing complications and containing costs [12]. Moreover, despite its requirement, the clinicians rarely define the type of infection and the presumable causative micro-organism before treating [13].

In developing countries, patients frequently waste scarce household resources on unnecessary antimicrobials therapy [14]. In these countries, antimicrobials are prescribed for 44-97% of hospitalized patients often unnecessarily or inappropriately [15]. Reasons for inappropriate antimicrobials prescriptions in hospitals include uncertainty of
differential diagnoses, complex co-morbidities, lack of training and/or experience, or confidence of physicians in charge, lack of knowledge of local epidemiology of antimicrobial resistance or wrong interpretation of microbiological results [16].

Although commonly practiced, inadequate antimicrobial regimen is ineffective and favours emergence of resistant strains [17]. Each year many patients are hospitalized with adverse drug reactions [18]. Reduction in antimicrobials consumption is clearly important to minimize this problem [19].

In Scandinavian countries Europe, data on the extent of use and type of prescribed antimicrobials as well as the information on antimicrobial resistance levels are continuously collected and analyzed and presented to doctors in primary health care [20]. However, antimicrobial resistance is a growing problem in developing countries [21].

In Ethiopia, there is no launched national controlling system or policy on antimicrobials use; neither do the hospitals including specialized hospitals have their own antimicrobial use guidelines or controlling systems to assure effective treatment and limit the use of broad-spectrum antimicrobials. Therefore, this study aimed to assess the magnitude and patterns of antimicrobial use problems and to identify the associated factors.

Methods and Participants

Study area and period

The study was conducted in Bonga, Teppi and Mizan general hospitals which are found in three bordering zones, Keffa, Sheka and Benchi Maji, south west Ethiopia from March 1-30, 2015. The areas have hot and humid climate with high annual rainfall.

Study design

A prospective observational study design was employed.

Populations

Source population: All patients admitted at medical wards of Bonga, Teppi and Mizan general hospitals

Target population: All patients admitted at medical wards of Bonga, Teppi and Mizan general hospitals who take antimicrobial(s) or who need one(s).

Study population: Patients admitted at medical wards of Bonga, Teppi and Mizan general hospitals during the study period that fulfilled inclusion and exclusion criteria.

Variables

Independent variables: Patient related:

- Patient age
- Patient sex
- Co-morbidities
- Concurrent medications
- Financial constraints
- Beliefs/Misconception

Prescriber/Facility/Drug related

- Status of the prescriber
- Timely laboratory results

Length of hospital stay
- CPGs
- Antimicrobial category
- Total number of drugs taken
- Availability of antimicrobials
- Medication history
- Availability of culture and sensitivity tests

Dependent variables

- Antimicrobial use problems

Inclusion and exclusion criteria

Inclusion criteria

- Patients on any form of antimicrobials
- Those who have indication for any form of antimicrobial(s) treatment, but not on one(s)
- Patients on anti-TB or ART who also take concurrent systemic antimicrobials
- Age greater or equal to 15 years

Exclusion criteria

- Patients who completed the treatment before or on first day of data collection
- Patients who were admitted for less than 24 h
- Patients on anti-tuberculosis, antiretroviral therapy, viral hepatitis therapy and topical antimicrobials

Data collection process and data quality assurance

Data collection tools: The antimicrobial therapy was reviewed to assure compliance with the recommendations of the national guidelines or evidence based international clinical guidelines. The charts of all hospitalized patients who received an antimicrobial agent was reviewed, and data on patient description, current diagnoses, co-morbidities and medications was recorded anonymously in a patient specific protocol using the pre-prepared data abstraction format. Each patient was then asked for compliance related problems and the responses filled to the same checklist.

Data collectors: Two trained pharmacists were involved in collecting the data using the prepared checklist under the supervision of a senior pharmacist in each of the three hospitals.

Pre-test: The data collection tools were pre-tested and checked for completeness and feasibility by the principal investigator before the data collection period for any need of possible amendments. This data, however, were not part of the study results.

Data quality management: To optimize the quality of data collection, the principal researcher closely monitored every steps of data collection throughout the data collection period. Moreover, the Investigators were also committed to resolve any problems faced by the data collectors timely. In addition, the checklists were rechecked by the Investigators for any missed, incorrect and unreadable information whilst collecting data.

Data analysis and interpretation

The Statistical Package for Social Science (SPSS) programs version
The determinants of antimicrobial use problems

The binary logistic regression shows that among all the variables studied, the use of at least one social drug (alcohol, tobacco, Khat or caffeine) [COR=2.519(1.372-4.626); p=0.003 at 95% C.I.], the total number of drugs used [COR=2.480(1.272-4.835); p=0.008 for ≥3 drugs and COR=4.454(2.014-9.849); p=0.000 for ≥5 drugs at 95% C.I.] and history of using antimicrobials in the previous 3 months [COR=2.689(1.325-5.456); p=0.006 at 95% C.I.] were significantly associated with occurrence of at least one antimicrobial use problem (Table 5).

When multivariate logistic regression was done, only the use of social drug [AOR=2.549(1.279-5.080) at 95% C.I.; p value=0.008], the use of antimicrobial in the previous 3 months [AOR=4.095(1.855-9.040) at 95% C.I.; p value=0.000] and the total number of drugs used [AOR=2.997(1.413-6.356); p value=0.004 for ≥3 drugs and AOR=4.653(1.985-10.906); p value=0.000 for ≥5 drugs at 95% C.I.] were independently associated with antimicrobial use problems (Table 6).

Discussion

In our current study conducted at 3 hospitals, Mizan Aman, Tepi and Bonga Shawo general hospitals, we identified that no culture and...
susceptibility test was done to guide antimicrobials use. This, in turn, might significantly increase the mortality rate from acute infections; lengthens hospital stays and increase individual patients as well as the health care cost as a whole and more importantly narrows the future alternatives of antimicrobials therapy.

Almost in 113 (38.8%) of the patients, there was uncertainty in the differential diagnosis of the infectious disease until the first antimicrobials were prescribed. This is mainly due to the shortage of resources including: timely laboratory results and radiology services and probably shortage of experts on infectious diseases.

The mortality ratio of 23(7.9%) in this study is lower compared to previous study in Jimma University specialized hospital of 12.6% in 2010 [22]. This might be due to the exclusion of non-infectious medical conditions or the gradual improvement in the quality of health care in the region.

At least one type of antimicrobial use problem was identified among 233(80.1%) while the antimicrobial use was appropriate only among the remaining 58(19.9%). This level of inappropriate use of antimicrobials is much higher compared to 332 (46.7%) patients in a study by Ceyhan et al. in Turkey [23] but comparable with inappropriateness of 184(73.3%) in Kyrgyzstan [15]. The former might be attributed to the lower quality of health care in Ethiopia, one of the poorest countries.

The most frequent drug therapy problem type was 'need for additional drug therapy' which accounted for 91(31.3%) of the patients compared to 1947(37.9%) of patients of all types of diseases and drugs in a study by Robert et al. [24]. This might be lower because the need for additional drug therapy most probably is higher for non-infectious and chronic diseases which were excluded from this study. The delay in initiation of effective antimicrobials in acutely ill patients might increase in-hospital mortality.

On the other hand, unnecessary antimicrobial therapy of 44(28.9%) in this study is comparable to 30% of unnecessary days of antimicrobial therapy in Cleveland [25]. Accordingly, there is high rate of unnecessary antimicrobials use mainly due to the use of duplicates of broad spectrum antimicrobials combinations whereas a single one or a narrower spectrum antimicrobial would be more reasonable and recommended. This using of unnecessarily broader spectrum and duplicates of antimicrobials with overlapping spectrum of activity and similar mechanism of action will clearly contribute for the emergence and dissemination of antimicrobial resistant microorganisms.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Response category</th>
<th>Frequency(N=152)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy or breast feeding</td>
<td>Pregnant/Breast feeding</td>
<td>31*</td>
<td>24.6</td>
</tr>
<tr>
<td></td>
<td>Not Pregnant/Breast feeding</td>
<td>95*</td>
<td>75.4</td>
</tr>
<tr>
<td></td>
<td>Not applicable</td>
<td>165</td>
<td>56.7</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>None</td>
<td>46</td>
<td>15.8</td>
</tr>
<tr>
<td></td>
<td>One</td>
<td>135</td>
<td>46.4</td>
</tr>
<tr>
<td></td>
<td>Two</td>
<td>66</td>
<td>22.7</td>
</tr>
<tr>
<td></td>
<td>Three</td>
<td>28</td>
<td>9.6</td>
</tr>
<tr>
<td></td>
<td>Four and above</td>
<td>16</td>
<td>5.5</td>
</tr>
<tr>
<td>Medication history</td>
<td>Yes</td>
<td>101</td>
<td>34.7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>190</td>
<td>65.3</td>
</tr>
<tr>
<td>Total drugs used</td>
<td>≤2</td>
<td>85</td>
<td>29.2</td>
</tr>
<tr>
<td></td>
<td>&gt;2</td>
<td>196</td>
<td>33</td>
</tr>
<tr>
<td>Hospital stay in days</td>
<td>06-Oct</td>
<td>78</td>
<td>26.8</td>
</tr>
<tr>
<td></td>
<td>≥11</td>
<td>72</td>
<td>24.7</td>
</tr>
<tr>
<td>Clinical outcome</td>
<td>Dead</td>
<td>23</td>
<td>7.9</td>
</tr>
<tr>
<td></td>
<td>Worsened</td>
<td>53</td>
<td>18.2</td>
</tr>
<tr>
<td></td>
<td>Improved</td>
<td>207</td>
<td>71.1</td>
</tr>
</tbody>
</table>

Table 3: Patient/Medical factors related to antimicrobials use among patients admitted to medical wards of Mizan Aman, Bonga and Tepi hospitals who were prescribed or needed antimicrobials, from June 10 to August 30, 2015.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total incidents</th>
<th>Patients experienced (N)</th>
<th>Prevalence (N %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needs additional antimicrobial/s</td>
<td>94</td>
<td>91</td>
<td>31.3</td>
</tr>
<tr>
<td>Dosage too low</td>
<td>71</td>
<td>65</td>
<td>22.4</td>
</tr>
<tr>
<td>Non compliance</td>
<td>72</td>
<td>63</td>
<td>21.7</td>
</tr>
<tr>
<td>Unnecessary antimicrobial/s</td>
<td>60</td>
<td>58</td>
<td>19.9</td>
</tr>
<tr>
<td>Ineffective antimicrobial/s</td>
<td>46</td>
<td>46</td>
<td>15.8</td>
</tr>
<tr>
<td>Dosage too high</td>
<td>46</td>
<td>46</td>
<td>15.8</td>
</tr>
<tr>
<td>Adverse Drug Reaction</td>
<td>22</td>
<td>22</td>
<td>7.6</td>
</tr>
<tr>
<td>Total antimicrobial use problems</td>
<td>380</td>
<td>233</td>
<td>80.1</td>
</tr>
</tbody>
</table>

Table 4: Types of antimicrobial use problems identified among patients admitted to medical wards of Mizan Aman, Bonga and Tepi hospitals who were prescribed or needed antimicrobials, from June 10 to August 30, 2015. N: Total number of patients in each category; N %: The percentage of patients in each category.
Moreover, the use of antimicrobials for non-infectious diseases such as, asthma exacerbation, heart failure, cor-pulmonale and non-infectious diarrhea in the absence any laboratory test suggesting the infection was found to be rampant. This practice does also significantly contribute for excessive use of antimicrobials further contributing for antimicrobial resistance.

The prevalence of ‘dose too low’ of 65(22.4%) of antimicrobials in this study is comparable with 1436(28%) of a large multi-centered study by Robert et al. [24]. In this study, the most common causes for ‘Dose too low’ were drug interactions, too low dose and shorter duration of antimicrobial therapy. These problems might contribute to the emergence of antimicrobial resistance.

The prevalence of non-compliance of 63(21.7%) in this study was found to be higher compared to 19(13.19%) in Jordan [26] probably...
due to the fact that the patients spend ‘out of pocket money’ on the health expenditures and buying drugs in the hospitals like any other hospitals in Ethiopia. Moreover, because of the low income level of the patients, non-compliance was mainly related to unaffordability, 50/63 (79.4%) in this study.

Similarly, the prevalence of ‘Ineffective AM therapy’ was 46(15.8%) which is much lower compared to 97 (32.9%) in Kyrgyzstan [15] and 71(49%) in Jordan [26]. The reason for this low rate of ‘ineffective antimicrobial therapy’ may be due to the high rate of the use of duplicates of broad spectrum antimicrobials in this study.

In this study the binary logistic regression shows that there is no significant association between the occurrence of antimicrobial use problem and socio-demographic variables including: age, sex, occupation, educational level and marital status. This is comparable with a study by Blix et al. which found that neither of age nor gender was an independent risk factor for the occurrence of DTPs [27].

On the other hand, a significant association [AOR=2.549(1.279-5.080) at 95% C.I.; p value=0.008] was observed between the use of at least one social drug (alcohol, tobacco, Khat or caffeine) and the probability of occurrence of at least one drug therapy problem. This might be attributed to the use of these unnecessary drugs by itself as well as the probable result of their uses on non-compliance and contribution for drug interaction.

Medication history, the use of antimicrobial in the previous 3 months was the other variable significantly associated [AOR=4.095(1.855-9.040) at 95% C.I.; p value=0.000] was the other identified determinant of antimicrobial use problem. This might be due to the fact that many prescribers did not assess and consider which antimicrobials the prescribers did not assess and consider which antimicrobials the patients had taken previously. However, the past antimicrobial therapy might positively or negatively affect the current selection by influencing the safety and effectiveness of current treatment.

Finally, the total number of drugs used was significantly associated [AOR=2.997(1.413-6.356); p value=0.004 for 3-4 drugs and AOR=4.653(1.985-10.906); p value=0.000 for ≥5 drugs at 95% C.I.] with antimicrobial use problems. A case that used 3-4 drugs and 5 or more drugs was about 2.997 and 4.653 times more likely to encounter these problems compared to those who used 2 or less drugs. This association might be explained by the fact that the more the number of drugs used, the higher the probability of drug interactions with possible effects on safety or efficacy or both as well as the possible increased probability of non-compliance due to inconvenience, safety or cost issues. For one example, failure to check for adverse drug interactions contributed for 25.5% of all the medication errors in a study in a tertiary hospital in Nigeria [28]. This association is comparable with a study by Blix et al. [29] and another study by Haugbølle and Sørensen [30] both of which independently showed DTPs increased with the increase in number of drugs used.

### Conclusion and Recommendations

#### Conclusion

Generally, the antimicrobials use problems in the medical wards of Mizan Aman, Tepi and Bonga Shawo hospitals is higher compared to most of the studies from developed countries but comparable to those in developing countries. At least one antimicrobial use problem was prevalent among most of the patients. Most of the problems were due to excessive use or delay of initiation of effective antimicrobials, lack of confirmation of infection, unaffordability of antimicrobial therapy and deviation in selection of antimicrobials from either national or the evidence based guidelines of IDSA. The independent determinants of antimicrobial use problems were the total number of drugs used, use of social drugs and the previous use of antimicrobials.

#### Recommendations

Each of the 3 hospitals should strengthen the microbiological services to help preventing antimicrobial resistance. The health professionals in the hospitals should manage how to accurately and comprehensively obtain medication history and prescribe accordingly. The local health sectors and collaborating NGOs should organize the effort towards raising public awareness on the determinant effects of social drugs and their effect on drug therapy. The hospitals DTCs should closely monitor the unnecessary duplications of drug therapies by strengthening clinical pharmacy services, providing due trainings and by devising strategies to promote rational use of antimicrobials and control the use.

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